

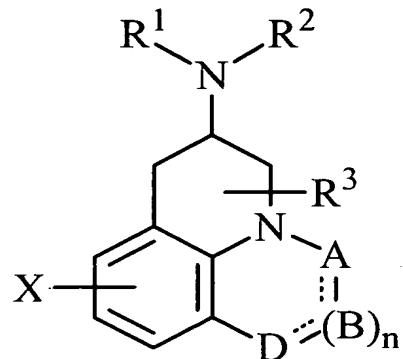
WHAT IS CLAIMED IS:

Ameliorating

1. A method of treating or suppressing the symptoms
5 of at least one disorder selected from addictive
disorders, psychoactive substance use disorders,
~~intoxication disorders, inhalation disorders, alcohol~~
addiction, tobacco addiction, and nicotine addiction,
said method comprising the step of administering a
10 therapeutically effective, nontoxic amount of an active
agent selected from the group consisting of a
heterocyclic amine, a phenylazacycloalkane, a
cabergoline, an aromatic bicyclic amine, and
pharmaceutically acceptable derivatives or salts of any
15 said active agent, to a patient in need of treatment.

*Wherein said active agent is a
het. amine*

2. The method of claim 1 wherein the active
agent is a heterocyclic amine of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

R¹, R², and R³ are each independently hydrogen, C₁₋₆ alkyl, C₃₋₅ alkenyl, C₃₋₅ alkynyl, C₃₋₇ cycloalkyl,

5 C₄₋₁₀ cycloalkyl- or phenyl- substituted C₁₋₆ alkyl, or R¹ and R² are joined to form a C₃₋₇ cyclic amine which can contain additional heteroatoms and/or unsaturation;

n is 0 or 1;

X is hydrogen, C₁₋₆ alkyl, halogen, hydroxy, alkoxy, 10 cyano, carboxamide, carboxyl, or carboalkoxyl;

A is CH, CH₂, CH-halogen, CHCH₃, C=O, C=S, C-SCH₃, C=NH, C-NH₂, C-NHCH₃, C-NHCOOCH₃, C-NHCN, SO₂, or N;

B is CH₂, CH, CH-halogen, C=O, N, NH, N-CH₃, or O; and

15 D is CH, CH₂, CH-halogen, C=O, O, N, NH, or N-CH₃.

3. The method of claim 2, wherein:

D is N or NH, n is 0, and R¹, R², R³, X, A, and B are as defined in claim 2; or

20 A is CH, CH₂, CHCH₃, C=O, C=S, C-SCH₃, C=NH, C-NH₂, C-NHCH₃, C-NHCOOCH₃, or C-NHCN, and R¹, R², R³, n, X, B, and D are as defined in claim 2; or

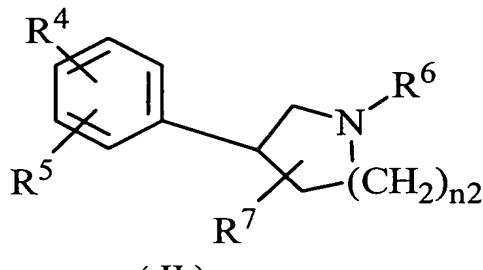
A is CH or C=O, and R¹, R², R³, n, X, B, and D are as defined in claim 2.

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4. The method of claim 2 wherein the active agent is selected from the group consisting of:

(5R)-5-(methylamino)-5,6-dihydro-4H-imidao[4,5,1-ij]quinolin-2(2H)-one;
(5R)-5-(methylamino)-5,6-dihydro-4H-imidazo[4,5,1-ij]quinoline-2(1H)-thione;
5 (5R)-5-(methylamino)-5,6-dihydro-4H-imidazo[4,5,1-ij]quinoline-2(1H)-thione maleate; and
(5R)-5-(methylamino)-5,6-dihydro-4H-imidazo[4,5,1-ij]quinoline-2(1H)-thione 2-butenedioanate.

10 5. The method of claim 1 wherein the active agent is a phenylazacycloalkane compound of the formula:



15

or a pharmaceutically acceptable salt thereof, wherein:

n2 is 0-3;

R⁴ and R⁵ are independently hydrogen, -OH, CN, CH₂CN,

2- CF_3 , 4- CF_3 , CH_2CF_3 , CH_2CHF_2 , $\text{CH}=\text{CF}_2$, $(\text{CH}_2)_2\text{CF}_3$, ethenyl,
2-propenyl, OSO_2CH_3 , OSO_2CF_3 , SSO_2CF_3 , COR^7 , COOR^7 , $\text{CON}(\text{R}^7)_2$,

$\text{SO}_{x_1}\text{CH}_3$, wherein x_1 is 0-2, $\text{SO}_{x_1}\text{CF}_3$, $\text{O}(\text{CH}_2)_{x_1}\text{CF}_3$, $\text{SO}_2\text{N}(\text{R}^7)_2$,

$\text{CH}=\text{NOR}^7$, COCOOR^7 , $\text{COCOON}(\text{R}^7)_2$, C_{1-8} alkyl, C_{3-8} cycloalkyl,

5 CH_2OR^7 , $\text{CH}_2(\text{R}^7)_2$, $\text{NR}^7\text{SO}_2\text{CF}_3$, NO_2 , halogen, a phenyl at
positions 2, 3 or 4, thienyl, furyl, pyrrole, oxazole,
thiazole, N-pyrroline, triazole, tetrazole or pyridine;
provided that at least one of R^4 and R^5 is a substituent
other than hydrogen and provided that when R^4 or R^5 is -OH

10 R^7 is other than hydrogen;

R^6 is hydrogen, CF_3 , CH_2CF_3 , C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{4-9} cycloalkyl-methyl, C_{2-8} alkenyl, C_{2-8} alkynyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl,
- $(\text{CH}_2)_m\text{R}^8$, wherein m is 1-8, CH_2SCH_3 or a C_{4-8} alkyl

15 bonded to said nitrogen and one of its adjacent carbon
atoms inclusive to form a heterocyclic structure;

R^7 is independently hydrogen, CF_3 , CH_2CF_3 , C_{1-8} alkyl,
 C_{3-8} cycloalkyl, C_{4-9} cycloalkyl-methyl, C_{2-8} alkenyl,
 C_{2-8} alkynyl, 3,3,3-trifluoropropyl,

20 4,4,4-trifluorobutyl, - $(\text{CH}_2)_m\text{R}^8$, wherein m is 1-8;

R^8 is phenyl optionally substituted with a CN , CF_3 ,
 CH_2CF_3 , C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{4-9} cycloalkyl-methyl, C_{2-8} alkenyl, C_{2-8} alkynyl,
2-thiophenyl, 3-thiophenyl, $-\text{NR}^9\text{CONR}^9\text{R}^{10}$, or $-\text{CONR}^9\text{R}^{10}$; and

25 R^9 and R^{10} are each independently hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{4-9} cycloalkylmethyl, C_{2-8}

alkenyl or C₂-C₈ alkynyl.

6. The method of claim 5 wherein:

R⁴ is CN, and n2, R⁵, R⁶, and R⁷ are as defined in
5 claim 5; or

R⁵ is H, R⁶ is n-propyl, and n2, R⁴, and R⁷ are as
defined in claim 5; or

R⁴ is -OSO₂CF₃, and n2 and R⁵-R⁷ are as defined in
claim 5; or

10 R⁵ is H, R⁶ is C₁₋₈ alkyl, and n2, R⁴, and R⁷ are as
defined in claim 5; or

R⁴ is 3-OH, R⁵ is H, R⁶ is n-propyl, R⁷ is a C₁₋₈
alkyl, and n is as defined in claim 5; or

n2 is 2, and R⁴-R⁷ are as defined in claim 5; or

15 n2 is 0, and R⁴-R⁷ are as defined in claim 5.

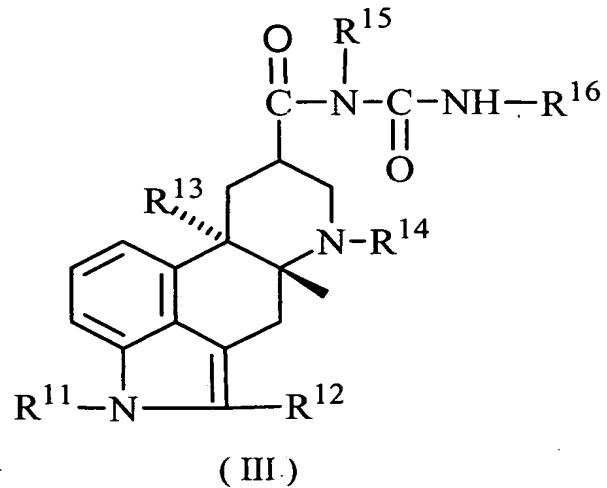
7. The method of claim 5 wherein the
phenylazacycloalkane compound is selected from the group
consisting of:

20 (3S)-3-[3-(methylsulfonyl)phenyl]-1-propylpiperidine
hydrochloride;

(3S)-3-[3-(methylsulfonyl)phenyl]-1-propylpiperidine
hydrobromide; and

(3S)-3-[3-methylsulfonyl]phenyl]-1-propylpiperidine
25 (2E)-2-butenedioate.

8. The method of claim 1 wherein the active agent
is a cabergoline of the formula:



5

10 or a pharmaceutically acceptable salt thereof, wherein:

R¹¹ is hydrogen or methyl;

R¹² is independently hydrogen, halogen, methyl,

formyl, S-R¹⁷, or SO-R¹⁷, wherein R¹⁷ is C₁-C₄ alkyl or phenyl;

R¹³ is hydrogen or methoxy;

R¹⁴ is independently C₁-C₄ alkyl, C₁-C₄ alkenyl, C₁-C₄ alkynyl, benzyl, or phenyl; and

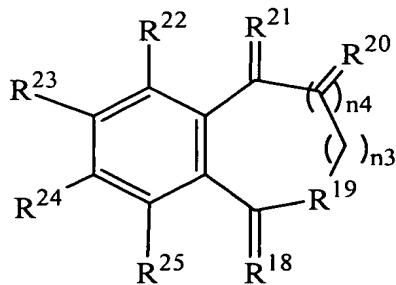
R¹⁵ and R¹⁶ are each independently C₁-C₄ alkyl, cyclohexyl, benzyl, phenyl optionally substituted with halogen or methoxy, or (CH₂)_{n3}N(CH₃)₂, wherein n3 is an integer.

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9. The method of claim 8 wherein the active agent is 1-((6-allylergolin-8 β -yl)carbonyl)-1-(3-(dimethylamino)propyl)-3-ethylurea.

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10. The method of claim 1 wherein the active agent is an aromatic bicyclic amine compound of the formula:



(IV)

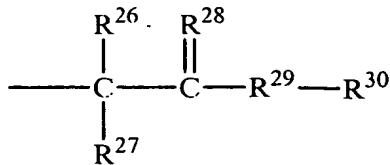
wherein:

n3 is 0 or 1;

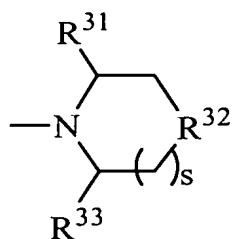
n4 is 0 or 1, provided that R²⁰ is not present when

n4 is 0;

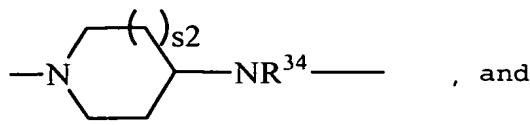
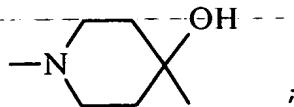
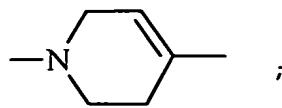
5 R¹⁸ is α -R¹⁸⁻¹: β -R¹⁸⁻² where one of R¹⁸⁻¹ or R¹⁸⁻² is selected from the group consisting of H or C₁-C₆ alkyl, and the other of R¹⁸⁻¹ or R¹⁸⁻² is a group of the formula:



wherein R²⁶ and R²⁷ are independently selected from H 10 or C₁-C₆-alkyl; R²⁸ is oxygen (O) or R²⁸ is α -R²⁸⁻¹: β -R²⁸⁻², wherein R²⁸⁻¹ and R²⁸⁻² are independently selected from H or C₁-C₆ alkyl; R²⁹ is selected from the group consisting of:



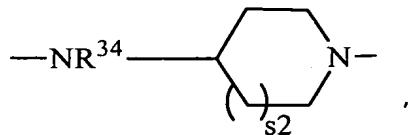
wherein R³¹ and R³³ are independently selected 15 from H or C₁-C₆ alkyl; R³² is nitrogen (N-) or methine (HC-); and s is 1 or 2;



, and

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5 wherein R^{34} is selected from the group consisting of H, C_1-C_6 alkyl, C_3-C_7 cycloalkyl, $-C_1-C_3$ alkyl- (C_3-C_7 cycloalkyl); and $s2$ is 0, 1, or 2;



wherein R^{34} and $s2$ are as defined above;

R^{19} is oxygen (O) or sulfur (S);

10 R^{20} is α - R^{20-1} : β - R^{20-1} , wherein one of R^{20-1} and R^{20-2} is H, C_1-C_6 alkyl, and the other of R^{20-1} or R^{20-2} is H, C_1-C_6 alkyl, phenyl, hydroxy, and $-O-(C_1-C_3$ alkyl);

R^{21} is α - R^{21-1} : β - R^{21-1} , wherein one of R^{21-1} and R^{21-2} is

H, C₁-C₆ alkyl, and the other of R²¹⁻¹ or R²¹⁻² is H, C₁-C₆ alkyl, phenyl, hydroxy, and -O-(C₁-C₃ alkyl); and when n₄ is 1, one of R²⁰⁻¹ or R²⁰⁻² and one of R²¹⁻¹ or R²¹⁻² can be taken together with the carbon atoms to which they are attached to form a carbon ring of 5-, 6-, or 7-members;

R²² is H, F, Cl, Br, I, -CONR³⁵R³⁶, -SONR³⁵R³⁶, CF₃, NR³⁵R³⁶, NO₂, CN, -NR³⁵-CO-R³⁶, -SO₂CF₃, C₁-C₄ alkyl, Si(CH₃)₃, and phenyl optionally substituted with one or two substituents selected from the group consisting of F, Cl, Br, I, and -CO-NR³⁵R³⁶, wherein R³⁵ and R³⁶ are independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, and -C₁-C₃ alkyl-(C₃-C₇ cycloalkyl);

and where R²² and one of R²¹⁻¹ or R²¹⁻² are taken together with the carbon atoms to which they are attached to form a carbon ring of 5-, 6-, or 7-members;

R²³ is H, F, Cl, Br, I, -CONR³⁷R³⁸, -SONR³⁷R³⁸, CF₃, NR³⁷R³⁸, NO₂, CN, -NR³⁷-CO-R³⁸, -SO₂CF₃, C₁-C₄ alkyl, Si(CH₃)₃, and phenyl optionally substituted with one or two substituents selected from the group consisting of F, Cl, Br, I, and -CO-NR³⁷R³⁸, wherein R³⁷ and R³⁸ are independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, and -C₁-C₃ alkyl-(C₃-C₇ cycloalkyl);

R²⁴ is H, F, Cl, Br, I, -CONR³⁹R⁴⁰, -SONR³⁹R⁴⁰, CF₃, NR³⁹R⁴⁰, NO₂, CN, -NR³⁹-CO-R⁴⁰, -SO₂CF₃, C₁-C₄ alkyl, Si(CH₃)₃, and phenyl optionally substituted with one or two substituents selected from the group consisting of F, Cl, Br, I, and -CO-NR³⁹R⁴⁰, wherein R³⁹ and R⁴⁰ are independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, and -C₁-C₃ alkyl-(C₃-C₇ cycloalkyl);

R²⁵ is H, F, Cl, Br, I, -CONR⁴¹R⁴², -SONR⁴¹R⁴², CF₃, NR⁴¹R⁴², NO₂, CN, -NR⁴¹-CO-R⁴², -SO₂CF₃, C₁-C₄ alkyl, Si(CH₃)₃,

and phenyl optionally substituted with one or two substituents selected from the group consisting of F, Cl, Br, I, and -CO-NR⁴¹R⁴², wherein R⁴¹ and R⁴² are independently selected from the group consisting of H, C₁-

5 C₆ alkyl, C₃-C₇ cycloalkyl, and -C₁-C₃ alkyl-(C₃-C₇ cycloalkyl);

with the proviso that not more than two of R²², R²³, R²⁴, and R²⁵ are other than H; and

R³⁰ is selected from the group consisting of:

10 phenyl optionally substituted with one or two substituents selected from the group consisting of CF₃, COR⁴³, COOR⁴³, CN, NO₂, NR⁴⁴-CO-R⁴⁵, -S-(C₁-C₆ alkyl), NR⁴⁴R⁴⁵, or a group represented by R⁴⁶;

15 2-, 3-, and 4-pyridinyl optionally substituted with one or two substituents represented by R⁴⁶; and

2-, 4-, and 5-pyrimidinyl optionally substituted with one or two substituents represented by R⁴⁶;

wherein R⁴³, R⁴⁴ and R⁴⁵ are independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₇

20 cycloalkyl,

-C₁-C₃ alkyl-(C₃-C₇ cycloalkyl); and R⁴⁶ is selected from the group consisting of F, Cl, Br, I, -CO-NR⁴⁴R⁴⁵, -SO₂NR⁴⁴R⁴⁵, OH, SH, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, -OR⁴⁷, -CH₂-(C₃-C₆ cycloalkyl), -CH₂-phenyl, C₃-C₆ cycloalkyl, -

25 SO₂CF₃, and

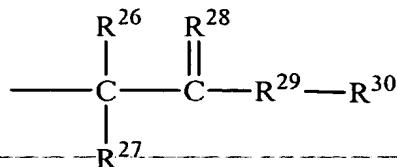
-CH₂CF₃, wherein R⁴⁴ and R⁴⁵ are as previously defined and R⁴⁷ is C₁-C₆ alkyl; and

enantiomers and diasteromers thereof, where such exist, and pharmaceutically acceptable salts thereof.

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11. The method of claim 10 wherein:

one of the substituents represented by R¹⁸⁻¹ or R¹⁸⁻² is H, and the other substituent represented by R¹⁸⁻¹ or R¹⁸⁻² is a group of the formula:



wherein R^{26} , R^{27} , R^{28} , R^{29} and R^{30} are as defined in claim 10.

5 12. The method of claim 10 wherein the active agent is selected from the group consisting of:

1- (4-fluorophenyl)-4-[2-(isochroman-1-yl)ethyl]piperazine;

1-[2-(isochroman-1-yl)ethyl]-4-phenylpiperazine;

10. 1-[2-(isochroman-1-yl)ethyl]-4-(4-methoxyphenyl)piperazine;

(-)-4-[4-[2-(isochroman-1-yl)ethyl]piperazin-1-yl]benzamide; and

15 (-)-4-[4-[2-(isochroman-1-yl)ethyl]piperazin-1-yl]benzenesulfonamide.

13. The method of claim 1 wherein the active agent is used to treat or enhance the treatment of tobacco and/or nicotine addiction.

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14. The method of claim 1 wherein the active agent is used to reduce the craving for tobacco and/or nicotine containing products.

25 15. The method of claim 1 wherein the active agent

is used to reduce the smoking and/or chewing of tobacco-
or nicotine-containing products.

16. The method of claim 1 wherein the active agent
5 is administered to the patient three times a day.

17. The method of claim 1 wherein the active agent
is selected from the group consisting of a heterocyclic
amine, a phenylazacycloalkane, and a cabergoline
10 administered in a dose of about 0.01 mg/day to about 10.0
mg/day.

18. The method of claim 17 wherein the active agent
is selected from the group consisting of a heterocyclic
15 amine, a phenylazacycloalkane, a cabergoline, and a
cabergoline-type derivative administered in a dose of
about 0.125 mg/day to about 6 mg/day.

19. The method of claim 18 wherein the active agent
20 is administered in an amount from about 0.375 mg/day to
about 5 mg/day.

20. The method of claim 19 wherein the active agent
is administered in an amount from about 0.75 mg/day to
25 about 4.5 mg/day.

21. The method of claim 17 wherein an initial dose
of active agent of about 0.125 mg/day administered to the
patient three times a day is titrated to higher levels
every five to seven days until therapeutic effect is
5 achieved.

22. The method of claim 1 wherein the active agent
is an aromatic bicyclic amine administered in an amount
of from about 5 mg/day to about 120 mg/day.

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23. The method of claim 22 wherein the aromatic
bicyclic amine is administered in an amount of from about
20 mg/day to about 100 mg/day.

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24. The method of claim 23 wherein the aromatic
bicyclic amine is administered in an amount of from about
40 mg/day to about 80 mg/day.

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25. The method of claim 22 wherein an initial dose
of active agent of about 5 mg/day is administered to the
patient three times a day and is titrated to higher
levels every five to seven days until therapeutic effect
is achieved.